

Effect of *Melothria maderaspatana* Leaf-Tea Consumption on Blood Pressure, Lipid Profile, Anthropometry, Fibrinogen, Bilirubin, and Albumin Levels in Patients with Hypertension

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ABSTRACT

Objective: To determine the effect of *Melothria maderaspatana* (Linn.) leaf-tea on blood pressure, plasma lipid profile, fibrinogen, albumin together with serum bilirubin and anthropometric measurements in volunteer participants with hypertension, because all these variables have been shown to influence vascular events.

Subjects and design: A total of 50 subjects—25 (mean age of 58 ± 9.0 years; 12 were women) with mild-to-moderate hypertension (systolic blood pressure [SBP] ≥ 140 mm Hg; diastolic blood pressure [DBP] ≥ 90 mm Hg) and 25 normotensives (mean age of 48 ± 8.0 years; 11 women)—were selected for this study. Plasma lipid profile, fibrinogen, albumin, serum bilirubin, and anthropometric measurements were measured at baseline and after leaf-tea consumption by the patient with hypertension for 45 days.

Results: SBP and DBP gradually decreased and pulse rate decreased. The total cholesterol, low-density lipoprotein cholesterol and triglycerides, and phospholipids levels decreased significantly and high-density lipoprotein cholesterol and serum bilirubin levels increased after tea consumption in patients with hypertension. We also observed significant body weight loss and reduction in fibrinogen levels. There was no significant difference in plasma level of albumin.

Conclusions: Thus, *M. maderaspatana* leaf-tea consumption gradually decreased BP and showed beneficial effects on blood lipid profile, fibrinogen, bilirubin, and body mass index in patients with hypertension.

INTRODUCTION

Hypertension and dyslipidemia are major risk factors of cardiovascular morbidity and mortality and a continuing challenge to public health efforts.¹ In addition, fibrinogen,^{2,3} reduced bilirubin,⁴ and albumin⁵ concentrations are also associated with an increased risk of developing cardiovascular diseases.

In modern society, herbal medicine continues to flourish and play a pivotal and indispensable role in public health care. Exploring the bioactive constituents represents a promising approach toward discovery of new drugs. Medicinal plants used in traditional folk medicine would be a

good source for this area of research. In India, different medicinal systems make use of a number of plants in the treatment of hypertension.

Melothria maderaspatana (heen kekiri) (Linn.) Cogn. Syn. *Mukia maderaspatana*, *Cucumis maderaspatana* or *Mukia scabrella* (family: Cucurbitaceae) is an annual monoecious herb, densely covered with white hairs. It is found throughout India ascending up to 1800 m in the hills. Folklore medicine claims that it is a good diuretic, stomachic,⁶ gentle aperient, antipyretic, and antipruritic,⁷ antiasthmatic, and antibronchitis besides its use in vertigo and biliousness.⁸ It is used in Ayurveda for various therapeutic purposes such as relief of toothache or flatulence, and as an expectorant

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and a sudorific. Certain traditional medical practitioners also use the leaf-tea of this plant for alleviation of jaundice.^{9,10} Decoctions of leaves of this plant have been used¹¹ by Siddha practitioners in Tamil Nadu for the treatment of hypertension. This plant leaf extract has also been shown to have hepatoprotective^{12,13} and immunomodulatory effects¹⁴⁻¹⁶ and antiarthritic activity properties.¹⁷ Furthermore, our earlier report showed that consumption of *M. maderaspatana* leaf-tea significantly attenuated blood pressure, strengthened blood antioxidant potential, and lowered glycoprotein components in patients with hypertension.¹⁸ However, no study has shown its effect toward lipid profile, fibrinogen, albumin, and bilirubin of patients with hypertension. Thus, the present study investigates the possible effects of *M. maderaspatana* leaf-tea on lipid profile, fibrinogen, albumin, and serum bilirubin, which provide a scientific basis for its antihypertensive property as claimed by many traditional healers.

MATERIALS AND METHODS

Study population and design

A total of 50 volunteer participants (25 with mild-to-moderate hypertension) with a mean age of 58 ± 9.0 years were enrolled in the study. Of these 25 patients with hypertension, 12 were women and 13 were men. All the patients with hypertension patients were recruited from the Siddha division of Government Kamaraj Hospital, Chidambaram, Tamil Nadu, India. The protocol was approved by the Ethics Committee of Annamalai University. Informed consent was obtained from all participants after a detailed explanation of protocol. All the patients showed a mean systolic blood pressure (≥ 140 mm Hg) or a mean diastolic blood pressure (≥ 90 mm Hg) or both on at least three occasions at the outpatient clinic. The possibility of secondary causes of hypertension was excluded through a comprehensive checkup including an assessment when needed. The patients completed a detailed health and lifestyle questionnaire, which includes alcohol intake, cigarette smoking, not under any antihypertensive medication, and regular physical activity. All the patients with hypertension were treated with leaf-tea for 45 days and blood pressure was measured every 15th day; 25 subjects (11 women and 14 men) with a mean age of 48 ± 8.0 years that showed no history of hypertension, diabetes mellitus, alcoholism, cigarette smoking, or any other chronic illness were selected as control subjects. Occupationally they were indulging in almost similar physical activities.

Plant material

Leaves of *M. maderaspatana* were collected from a local market of Chidambaram, Tamil Nadu and the plant was botanically authenticated. A voucher specimen (AU-6054)

of the plant has been deposited at the Herbarium of the Department of Botany, Annamalai University, Annamalainagar, Tamil Nadu. The dried leaves were made into fine powder with an auto-mix blender and were kept separately in an airtight container until the time of use. The leaf powder was added in hot water just before use. Two teaspoonfuls (2.0 ± 0.5 g) of the dry plant leaf powder were placed in 50 mL of hot water for 5 minutes and a tea was filtered through a cloth. Each patient, twice a day, consumed this tea-cloth-filtered leaf-tea for 45 days.

Blood pressure measurements

Blood pressure was measured by the same physician using a standard mercury sphygmomanometer (Ergometer 3000, Wall model; Richard Kallmeyer, Nachforschung, Bad Tolz, Germany). Subjects sat quietly for 10 minutes before the blood pressure measurements without talking, with the legs uncrossed and with the arm supported at heart level. Measurements were repeated three times, and the average of the last two measures was used in the analyses. Blood pressure was measured between 8:00 AM and 10:00 AM. Systolic blood pressure was recorded at the first appearance (Phase I) and diastolic blood pressure at the disappearance (Phase V) of Korotkoff's sounds.

Anthropometric measurements

Body weight was measured using an electronic scale while the subjects were without shoes and wearing light clothing, and height was measured with a stadiometer. Body-mass index (BMI) was calculated with the following formula: $BMI = \text{weight (kg)}/\text{height (m)}^2$.

Biochemical analysis

After patients fasted for 12 hours, a venous blood sample was collected from the antecubital vein of each seated participant and was distributed into heparin, sodium citrate, and plain tubes. The plasma and serum were separated and stored at 4°C until analysis.

Plasma total cholesterol (TC) was measured by the Siedel method¹⁹ and high-density lipoprotein (HDL)-C by the same method in the supernatant after precipitation with phosphotungstic acid-magnesium chloride. Low-density lipoprotein (LDL)-C was calculated by the Friedwald formula.²⁰ Plasma triglycerides,²¹ free fatty acids,²² phospholipids,²³ fibrinogen,²⁴ albumin,²⁵ and serum bilirubin²⁶ were measured.

Statistical analysis

Statistical analysis was performed by using SPSS for Windows, version 10.0 (SPSS Software, Inc., Chicago, IL). The data were expressed as means \pm standard deviation. The data were analyzed using a paired *t* test, and the results were considered significant if the *p* values were <0.05 .

RESULTS

Table 1 shows the effect of *M. maderaspatana* leaf-tea on systolic and diastolic blood pressure in patients with hypertension at basal and after 45-day treatment with leaf-tea and in normotensives. Significant reduction was observed in both systolic and diastolic blood pressure ($p < 0.001$) on treatment with leaf-tea. Pulse rate increased in patients with hypertension and decreased after treatment. Table 1 also shows the effect of *M. maderaspatana* leaf-tea on height, weight, and BMI. There was significant weight loss and decrease in BMI in patients with hypertension after 45-day tea consumption.

Table 2 shows the levels of lipid profile in patients with hypertension treated with leaf-tea and in normotensives. An increased TC, LDL-C, plasma triglycerides (TG), free fatty acids (FFA), and phospholipids (PL) concentrations and decreased HDL-C concentration were observed in hypertensive patients. A significant decrease was noted in TC, LDL-C, TG, FFA, and PL, and HDL-C increased after tea consumption.

Table 3 shows the levels of fibrinogen, albumin and serum bilirubin in patients with hypertension before and after treatment with leaf-tea and in normotensives. Patients with hypertension had an elevated level of fibrinogen and a lowered level of serum bilirubin when compared to normotensives. There was no significant difference observed in the levels of albumin. A significant decrease in plasma fibrinogen level and increase in serum bilirubin levels were observed after tea consumption. We did not receive any reports on or find any adverse effects on the patients either during or after the treatment period.

DISCUSSION

The investigation of medicinal plants used as remedies in traditional folk medicine can be a useful tool to identify several biologically active molecules.²⁷ Information and the validation of such therapies have moved from a traditional

folklore to conventional scientific laboratory analysis and clinical research studies.

M. maderaspatana leaves have been used in Siddha and Ayurvedic medicine for more than 3 centuries. The entire leaf extract contains several phytochemicals, including spinasterol, 22,23-dihydrospinasterol, β -sitosterol, decosaenoic acid, triterpenes, phenolic compounds, and multiple glycosides (22,23-dihydrospinasterol-3-O- β -D-glucoside).^{28,29} A significant reduction of both systolic and diastolic blood pressure was observed in hypertensive patients after leaf-tea consumption. It shows that one or few principle of the leaf-tea act as vasodilator, lowering blood pressure. An *in vitro* study showed that the leaf extract of *M. maderaspatana* caused relaxation of isolated rat aorta endothelium, and the relaxant activity was independent of the integrity of the vascular endothelium.^{28,29} Stevens et al.³⁰ demonstrated that weight loss alone results in statistically and clinically significant improvements in blood pressure. Significant weight loss and lower BMI observed in our study may also be responsible for blood pressure reduction.

Abnormalities in plasma lipids and lipoprotein metabolism play a central role in the pathogenesis of hypertension. The presence of hyperlipidemia is so common in patients with hypertension that many have argued that the high blood pressure itself may play a role in altering lipid metabolism, resulting in abnormalities.³⁰ Our results showed a decrease in the levels of TC, TG, LDL-C, FFA, and PL in patients with hypertension after consumption of leaf-tea. An interesting observation was that the tea seemed to lower LDL-cholesterol and increase HDL-cholesterol. A number of publications support the concept that a low-dose supplementation of phytosterols is sufficient to produce significantly lower plasma cholesterol concentrations.^{31,32} The effect of spinasterol on reducing plasma and liver cholesterol levels has been recognized for many years. These sterols reduce cholesterol absorption by competing with cholesterol for uptake into mixed micelles and reduced absorption stimulates LDL receptor formation which, in turn, increases the hepatic uptake of LDL and thus decreases LDL-C levels.³³

PL are vital components of biomembrane. These PL and

TABLE 1. EFFECT OF *MELOTHRIA MADERASPATANA* LEAF-TEA ON BLOOD PRESSURE, PULSE RATE AND ANTHROPOMETRIC MEASUREMENTS IN HYPERTENSIVE PATIENTS

Parameters	Normotensives (n = 25)	Patients with hypertension (n = 25)		0 d vs. 45 d p
		0 day treatment	45th day treatment	
SBP mm Hg	127.4 \pm 12.53	159.4 \pm 9.02	135.6 \pm 7.07	<0.001
DBP mm Hg	82.5 \pm 8.16	101.0 \pm 7.88	85.5 \pm 5.87	<0.001
Pulse rate (bpm)	68.00 \pm 8.0	81.0 \pm 15.0	72.0 \pm 13.0	<0.05
Height (cm)	161.02 \pm 5.21	163.22 \pm 6.11	—	—
Weight (kg)	59.07 \pm 3.03	66.20 \pm 4.58	61.16 \pm 5.02	<0.001
BMI (kg/m ²)	22.00 \pm 2.41	24.98 \pm 3.14	22.61 \pm 2.28	<0.05

Values represent means \pm standard deviation. SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body-mass index.

TABLE 2. LEVELS OF LIPID PROFILES OF HYPERTENSIVE PATIENT ON TREATMENT WITH *MELOTHRIA MADERASPATANA*

Parameters	Normotensives (n = 25)	Patients with hypertension (n = 25)		0 d vs. 45 d p
		0 day treatment	45th day treatment	
TC (mg/dL)	170.63 ± 9.35	201.99 ± 9.80	185.66 ± 7.25	<0.001
HDL-C (mg/dL)	45.26 ± 3.38	36.04 ± 3.47	38.22 ± 3.46	<0.05
LDL-C (mg/dL)	105.59 ± 8.47	131.46 ± 10.39	118.66 ± 8.46	<0.001
VLDL-C (mg/dL)	20.22 ± 2.09	34.49 ± 2.26	28.78 ± 1.84	<0.05
TC/HDL-C	3.79 ± 0.30	5.62 ± 0.53	4.89 ± 0.46	<0.001
TG (mg/dL)	101.11 ± 10.47	172.41 ± 11.28	143.90 ± 9.21	<0.001
FFA (mg/dL)	18.69 ± 3.22	30.85 ± 3.13	26.65 ± 3.55	<0.001
PL (mg/dL)	155.73 ± 5.51	170.83 ± 8.41	161.06 ± 7.71	<0.001

Values represent means ± standard deviation. TC, total cholesterol; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein; TG, triglycerides; FFA, free fatty acids; PL, phospholipids.

FFA are important for the maintenance of cellular integrity, microviscosity, and survival.³⁴ Increased levels of plasma PL and FFA were observed in patients with hypertension, which might be due to membrane damage caused by increased lipid peroxidation. Increased lipid peroxidation is thought to be a consequence of oxidative stress that occurs when the dynamic balance between pro-oxidant and antioxidant mechanism is impaired.³⁵ *M. maderaspatana* is also being recognized as a potent antioxidant.^{16,18} Increased antioxidant levels may decrease lipid peroxidation, thereby preventing membrane damage that leads to decreased plasma PL and FFA level, in our study.

Numerous cross-sectional epidemiologic studies^{36–38} have reported a modest positive association between plasma fibrinogen levels and blood pressure. Perhaps augmented synthesis of fibrinogen may be due to increased utilization during mechanical injury caused by hypertension. Some experimental evidence suggests that administering pharmacologic agents to lower blood pressure can reduce fibrinogen levels or blood viscosity;^{39,40} this also implies that high blood pressure may raise hemorrheologic parameters, rather than vice versa. Plasma fibrinogen concentration depends on the rate at which it is secreted into the blood from the liver

where it is synthesized and on the rate of its elimination from the blood. This is either through the removal of intact fibrinogen by different organs; by its degradation in the blood to soluble products; or by conversion into and deposition as insoluble fibrin.⁴¹ Significant reduction in fibrinogen level was observed in patients with hypertension after tea consumption. Probably, tea may facilitate uptake and degradation of plasma fibrinogen by the organs, thereby decreasing the plasma fibrinogen.

Bilirubin, a bile pigment, acts as a potent physiologic antioxidant that may provide important protection against coronary artery disease.⁴² The lower serum bilirubin levels in the untreated hypertensive patients support the evidence of increased oxidant load in these patients.^{43,44} The significant increase of serum bilirubin level in the tea-consuming patients with hypertension in our study was compatible with the increased antioxidants level we reported previously^{16,18} from the leaf-tea. The plasma albumin concentration is a result of its rates of synthesis and degradation/excretion and its distribution between intra- and extravascular compartments.⁴⁵ There was no significant difference observed in the levels of albumin before and after tea consumption.

TABLE 3. LEVELS OF FIBRINOGEN, BILIRUBIN AND ALBUMIN IN HYPERTENSIVE PATIENT ON TREATMENT WITH *MELOTHRIA MADERASPATANA*

Parameters	Normotensives (n = 25)	Patients with hypertension (n = 25)		0 d vs. 45 d p
		0 day treatment	45th day treatment	
Fibrinogen (mg/dL)	208.78 ± 12.63	315.85 ± 14.99	298.44 ± 12.21	<0.001
Bilirubin (mg/dL)	0.98 ± 0.13	0.78 ± 0.09	0.88 ± 0.09	<0.001
Albumin (g/dL)	4.79 ± 0.10	4.74 ± 0.11	4.75 ± 0.11	NS

Values represent means ± standard deviation. NS, not significant.

CONCLUSIONS

Thus, *M. maderaspatana* leaf-tea consumption brings blood pressure to near normalcy, strengthens blood lipid profile, and showed beneficial effects on fibrinogen and bilirubin levels in patients with hypertension, which provide a pharmacologic basis for the traditional use of this plant.

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